Humanistic and Economic Burden of Pyruvate Kinase Deficiency: A Systematic Review of Literature

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Background & Objectives

Background: PKD is a rare, hereditary, chronic condition which is caused by mutations in the PKLR gene. It results in decreased activity of the erythrocyte isoform of PK which catalyzes the final step in glycolysis during which energy is released in the form of ATP. This enzyme deficiency shortens the lifespan of RBC, leading to lifelong hemolytic anemia.

Objective: To identify the published literature assessing humanistic and economic burden of PKD.

Methods

- A literature search was conducted in Embase® and MEDLINE® in May 2022 to identify relevant articles reporting the HRQoL and EB of PKD
- Studies were included if they were published in English. No further restrictions were applied
- Abstracts and full texts of records from databases were screened by two independent reviewers and conflicts relating to eligibility were resolved by a third reviewer (Figure1)
- Data was extracted and quality checked by independent reviewers

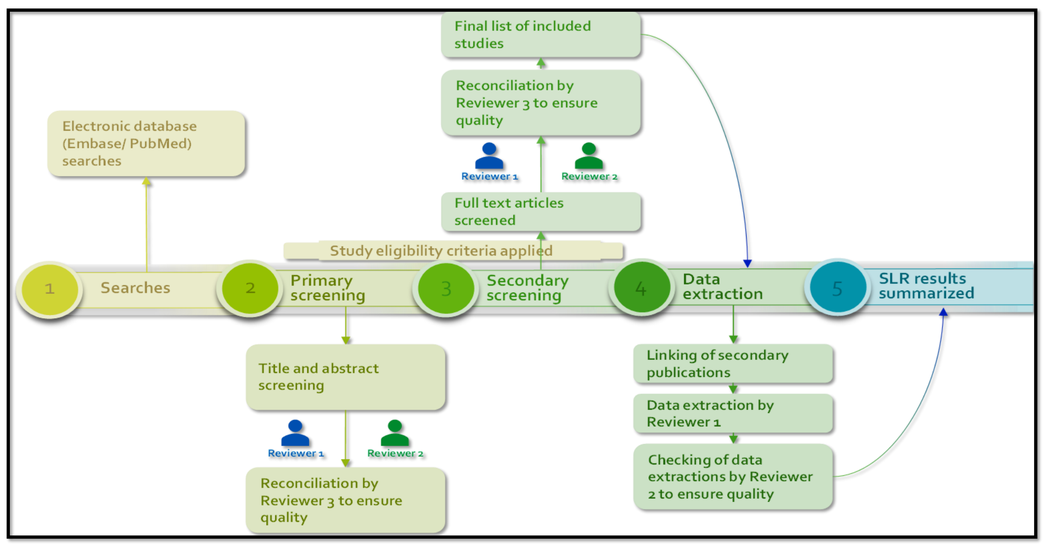

Figure 1. Selection Process for SLR

Summary of HRQoL Studies (n=7) [1-7]

- Most of the studies used generalized QOL measures like Fact-An or EuroQoL-5D or ADL (5/7; 71.4%). Only 2 studies used disease specific measures namely PKDD and PKDIA (2/7; 28.6%); figure 3

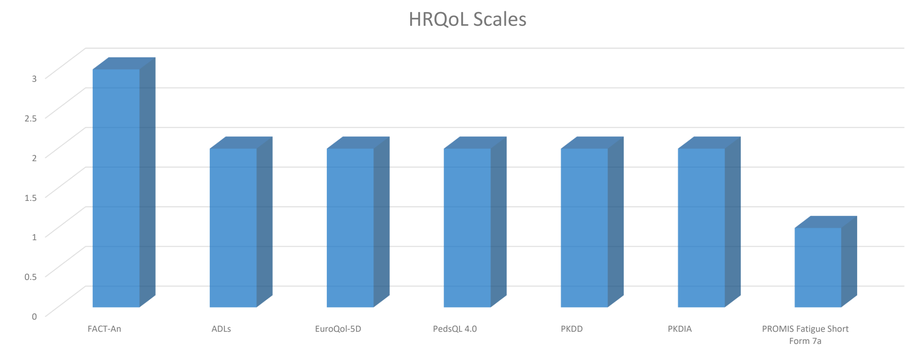

Figure 3. HRQoLs measures identified

- Six[1-6] included adult patients, while one[7] discussed pediatric population only
- All the six studies with adult patients reported that HRQoL is lower in RT patients
- HRQoL and fatigue significantly differed in children by genotype, with the worst scores in those with two severe PKLR mutations; this difference was not seen in adults
- Iron chelation was associated with significantly worse HRQoL scores in both children and adults

Summary of EB Study (n=1)[8]

- US payer perspective
- Direct healthcare costs only
- Time horizon of 100 years
- All costs standardized to 2020 US dollars

Abbreviations: ATP: Adenosine triphosphate; EB: Economic Burden; EuroQoL 5D: EuroQoL Five-Dimension Questionnaire; HRQoL: Health-related Quality of Life; NRT: Not regularly transfused; NT: Not Transfused, PKD: Pyruvate Kinase Deficiency; PKDD: The PK Deficiency Diary, PKDIA: PK Deficiency Impact Assessment; PedsQL 4.0: Pediatric Quality of Life; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROMIS: Patient Reported Outcomes Measurement Information System; RT: Regularly Transfused

Results

Of the identified 413 records, 367 were unique and eight[1-8] were included (see Figure 2).

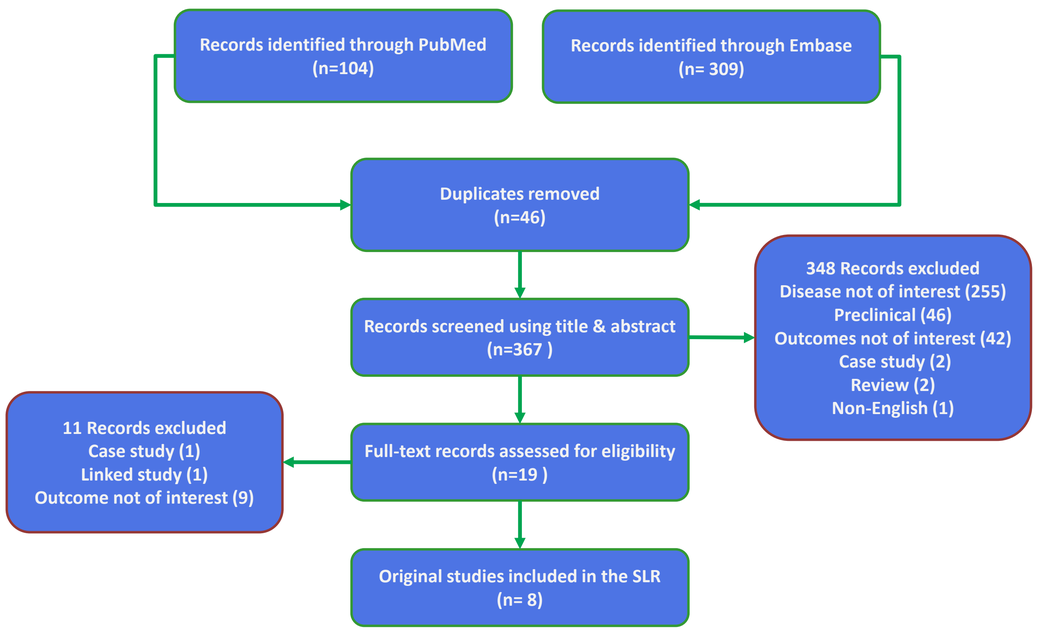

Figure 2. PRISMA flow diagram

Conclusions

- The identified evidence concluded that for assessing humanistic burden in PKD, disease specific tools like PKDD and PKDIA are more effective than generic tools for measurement of HRQoL
- Additionally, social/family support is an important factor for improved HRQoL. Improving social support could be an interesting future focus to increase HRQoL, especially in older, transfusion dependent patients
- HRQoL is lower in RT patients because they reported lower physical, emotional, and functional well-being and more anemia symptoms
- Direct cost involve the cost and frequency of transfusions and chelation therapies, and indirect costs include the cost associated with complications
- Therefore, EB is higher in all RT, NRT or NT populations, irrespective of the age group
- The lifetime EB of PKD from the perspective of the healthcare payer is substantial in both pediatric and adult populations

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